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Understanding tamoxifen adherence in women with breast cancer: a qualitative study

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Abstract

Objective: Non-adherence to tamoxifen is common in breast cancer survivors and is associated with poor clinical outcomes. This study aimed to understand women's experiences of taking tamoxifen and to identify factors which may be associated with non-adherence.

Design: A qualitative study using semi-structured interviews.

Methods: Thirty-two breast cancer survivors who had been prescribed tamoxifen took part in interviews conducted face to face or over the telephone. They were transcribed verbatim, and analysed using inductive thematic analysis with elements of grounded theory.

Results: A key theme identified in the data was *weighing up costs and benefits of treatment*, which resulted in women falling into three groups; *tamoxifen is keeping me alive*, *tamoxifen is not worth the reduced risk of recurrence*, or *conflicting beliefs about*

the harms and benefits of treatment. Additional themes were *living with risk of recurrence* and *information & support*.

Conclusions: Women who believed that the necessity of tamoxifen outweighed its costs were more likely to be adherent, whereas women who thought that the benefits did not outweigh the side-effects were more likely to have discontinued. A third more ambivalent group believed strongly in the importance of treatment, but were struggling with side-effects and were often non-adherent. Patients sometimes felt unsupported and discussed a need for more comprehensive information. To increase adherence, future research needs to explore ways to increase beliefs around tamoxifen necessity and how to help women cope with side-effects.

Introduction

Breast cancer is the most common cancer among women worldwide with around 1.7 million women diagnosed per year (American Cancer Society, 2015). Over three quarters of these breast cancers are oestrogen receptor positive (ER+), which means that the cancer cells are stimulated by the hormone oestrogen (Harrell et al., 2007). Hormonal therapies (HT) such as tamoxifen are prescribed to female breast cancer survivors in order to reduce the risk of the cancer returning by blocking oestrogen receptors in cancer cells. They are one of the most effective systemic treatments for ER+ positive breast cancer and can almost halve the rate of recurrence (Aguilar et al., 2010; Early Breast Cancer Trialists' Collaborative Group, 1998). Recent research has suggested that extending the prescription from five to ten years brings additional clinical benefits (Davies et al., 2013).

Despite this, many women do not take their treatment in accordance with agreed recommendations from their healthcare provider which is termed as non-adherence by the World Health Organisation (Sabaté, 2003). Non-adherence can consist of missing or altering doses and/or taking medication “holidays”. Non-adherence can be intentional, where the patient makes a deliberate decision not to take the medication as prescribed, unintentional where the patient may forget or not understand the instructions, or a combination of both. Some women also stop treatment completely before the recommended duration of five to ten years, which is known as non-persistence or discontinuation. Both non-adherence and non-persistence are associated with increased risk of breast cancer recurrence and mortality (Barron, Cahir, Sharp, & Bennett, 2013; Hershman et al., 2011). Studies show that by the fifth year of treatment, up to 50% of women have discontinued (Hadji et al., 2013; Owusu et al., 2008). Adherence rates

range over the course of treatment from 41-88% (Murphy, Bartholomew, Carpentier, Bluethmann, & Vernon, 2012) and fall to 50% by the fifth year of treatment (Lee et al., 2014; Partridge, 2003). As non-adherence and non-persistence have similar effects on clinical outcomes, they will both be referred to as “(non)-adherence” when discussing the implication of the research. This is consistent with taxonomies of adherence which define non-persistence as a type of non-adherence (Helmy et al., 2017; Vrijens et al., 2012).

Whilst there has been an attempt to understand the reasons for non-adherence, the majority of research has focussed on clinical and demographic factors, with few consistent predictors identified (Moon et al., 2017; Murphy, et al., 2012). Improving adherence rates is increasingly important as tamoxifen is now being prescribed for up to ten years instead of five years (Burstein et al., 2014) and is recommended as prophylaxis for women at high risk of breast cancer (NICE, 2013).

Tamoxifen lowers circulating oestrogen levels and as a result, is associated with a wide range of menopausal side effects. Hot flushes and night sweats are prevalent, occurring in around 80% of women taking tamoxifen (Moon et al., 2016). Other common menopausal side effects include loss of libido, fatigue, vaginal dryness and weight gain, which occur in more than one in ten women. Changes to mood and irritability are reported in 11% - 67% of patients taking tamoxifen (Cella & Fallowfield, 2008; Moon et al., 2016). Tamoxifen is often prescribed to younger, pre-menopausal women, many of whom would not normally be experiencing menopausal symptoms. Non-adherence is often assumed to be driven by these side effects (Demissie, Silliman, & Lash, 2001; Lash, Fox, Westrup, Fink, & Silliman, 2006), however little research has investigated empirically if this is the case. Whilst a small number of qualitative studies have been

conducted with breast cancer survivors taking adjuvant HT, researchers have highlighted a need to conduct more research to understand the complex problem of non-adherence and to develop interventions to increase adherence (Harrow et al., 2014; Verbrugghe, Verhaeghe, Lauwaert, Beeckman, & Van Hecke, 2013). One qualitative study found that women struggled with their understanding of the hormonal nature of tamoxifen (Pellegrini et al., 2010). Another found that many women suffered side effects which reduced their quality of life (QOL), but did not affect adherence (Harrow, et al., 2014), contradicting assumptions that side-effects resulted in non-adherence. However, non-adherent women and those who were premenopausal were under-represented in this study. Another study interviewed women prescribed HT and found that patients were surprised by the wide range of side effects they experienced (Van Londen et al., 2014). They were offered little support with coping with the side effects and had to develop strategies of their own. Verbrugghe et al. (2015) found that expectations regarding tamoxifen, information and social support contributed to HT non-adherence.

This previous research provides insight into the experiences of women prescribed HT, but the studies tended to focus more on the experiences of side effects and less on understanding if and how non-adherence is impacted by side-effects. Furthermore, the majority of previous research has investigated tamoxifen jointly with aromatase inhibitors, which have a significantly different side effect profile (Howell et al., 2005) and are usually prescribed to older, post-menopausal women. More research is needed to understand why women may not adhere to tamoxifen treatment, in order to develop ways to improve adherence. This research aimed to use an inductive qualitative approach to elicit a broad understanding of women's lived experiences of tamoxifen,

their motivation to adhere to treatment and identify reasons for non-adherence and non-persistence, in their own words. A better understanding of adherence and non-adherence in this population will provide invaluable knowledge for clinicians, but will also contribute to the design and development of interventions to improve both adherence and quality of life in women taking tamoxifen.

Methods

Participants

The study was approved by the Northampton National Research Ethics Committee (REF 14/EM/1207). Patients were eligible if they had been prescribed tamoxifen for a breast cancer diagnosis, were female, over 18, spoke fluent English, and able to consent for themselves. Participants were recruited from a London breast clinic, local support centres and through online advertisements to ensure a range of menopausal status at diagnosis and treatment durations.

Twenty-one women were approached in clinic and given information about the study. After being given two days to decide if they wanted to participate, these patients were contacted by the researcher. Twelve agreed to participate in the study. The remaining women could not be contacted. Online advertisements were placed on the following websites: Facebook; Macmillan Online Community; Asian Women's Breast Cancer Group; and Cancer Research UK Cancer Chat. Twenty-one women responded to these advertisements, were screened for eligibility and given information about the study. One woman declined to take part and interviews were arranged with the remaining twenty participants. Recruitment continued until data saturation was reached, defined as the point at which no new themes emerged.

Participants were all female, aged from 36 to 77 (mean=55, SD=10.6) (Table 1). Treatment duration ranged from 2 months to 6 years, with a mean duration of 23 months (SD=20). Thirty-eight percent of participants were in their first year of treatment.

Procedure

Clinic patients were told about the research by their clinician, and then introduced to a researcher. The researcher then gave the patient verbal information and an information sheet to take away. Patients were interviewed face to face in a private room or over the telephone. Informed consent was obtained prior to each interview. The interviews were based on a semi-structured interview schedule (Table 2). Questions were open ended and patients were encouraged to bring up issues which felt important to them. Patients were told that the researchers were interested in hearing their experiences regardless of whether they were currently taking their medication. Interviews were audio recorded and transcribed verbatim. Two researchers carried out the interviews.

Table 2 Interview schedule

Interview Questions	Prompts
General Questions	
How long have you been taking tamoxifen for?	
Do you know which brand you were taking?	
When were you diagnosed with breast cancer?	
Experiences of taking tamoxifen	Side effects? How do you cope with side effects?
Tell me about the experience of taking tamoxifen?	Family life?
Has anything changed over time?	Work life?
What would you change about tamoxifen?	Social life?
Adherence	How / when do you take it?
Tell me about the practical side of taking tamoxifen?	How do you remember to take it?
	How often do you take it?
Knowledge about tamoxifen	
What is your understanding of why you are taking tamoxifen?	Prior beliefs / expectations
	Treatment benefits
How long will you keep taking tamoxifen?	Concerns
Prescription process	
Tell me about how you were prescribed tamoxifen?	Who / when?
	What information were you given?
	Relationship with this person?
Overall	
Do you have anything else to add?	
Do you have any tips for other women prescribed tamoxifen?	

Data analysis

The interviews were anonymised and pseudonyms applied before being transcribed by a professional transcription company. All transcripts were checked against the recordings for accuracy. The interviews were analysed using thematic analysis, as described by Braun and Clarke (2006), incorporating elements of grounded theory (Glaser & Strauss, 2009). Data-analysis methods were chosen to optimise validity of the data and to develop a coherent picture of the patient's experiences. Inductive thematic analysis is a theoretically flexible approach which allows in-depth exploration of interviewees' experiences and perceptions with data-driven identification of patterns without preconceived assumptions of predefined theories or frameworks (Braun & Clarke, 2014). Elements of grounded theory were used to develop links between themes and provide a richer interpretation of the data.

After familiarisation with the data, one author generated initial codes, working systematically through the data set. Codes were based on language used by the participants and were applied to each new unit of meaning. Codes were organised into potential themes using thematic maps and tables following discussions with all authors. Themes were internally consistent, coherent and distinctive and were mapped onto the study aims. Following grounded theory, patterns and links between themes were developed in order to move beyond a purely descriptive analysis and to generate a theory within which to understand the data. Codes and themes were discussed within the research team and were modified until a coherent pattern of themes was identified. Transcripts were re-read to ensure the analysis was grounded in the data, that all items had been given equal attention and to ensure no data had been missed. Analysis was

iterative and involved constant comparison; a technique key to both thematic analysis and grounded theory which involves data, codes and themes being constantly compared.

Characterising patients as adherent

For the purpose of analysis, women were categorised as adherent or non-adherent (Table 1) based on information given in the interviews, after being explicitly asked about their medication taking behaviour. Women were considered adherent if they spoke about taking all or nearly all of their medication and non-adherent if they regularly skipped or halved the medication, or took treatment breaks. A few women self-reported having discontinued treatment. Women spoke consistently and explicitly about their medication taking behaviour, specifying if they forgot or skipped doses, which facilitated categorisation. For example, non-adherent women spoke about halving doses (e.g. *“So I’ve had breaks off it and then I’d go on...because you’re meant to take twenty milligrams a day. I’d do half doses like ten milligrams instead.”*) whereas adherent women spoke about never missing doses (e.g. *“I never forget to take it. If I do, everybody says have you taken your tablet, have you taken your tablet?”*). Two researchers independently classified women and there was 100% concordance between ratings. Two researchers also listed side effects experienced and classified women as experiencing mild, moderate or severe side effects based on their discussion of the impact of the side effects on their QOL. Agreement was 97% for the rating of severity and 89% for the list of side effects experienced. All discrepancies were resolved after discussion.

Table 1: Clinical and demographic characteristics of participants (n=32)

Pseudonym	Age	Menopausal status (at diagnosis)	Ethnic group	Time on tamoxifen	Adherence	Side effects
Sylvie	52	Post	White	2 years	Discontinued	Severe: HF, mood changes, poor sleep
Mary	49	Pre	White	6 months	Adherent	Mild
Elisabeth	37	Unsure	White	5 months	Adherent	Mild / moderate
Arlene	62	Post	White	2 years	Adherent	Moderate / Severe
Lisa	55	Peri	White	3 months	Adherent	Moderate
Holly	51	Peri	White	4 months	Adherent	None
Emma	45	Pre	White	1 year, 2 months	Adherent	Mild
Katie	56	Post	White	4 months	Adherent	Mild / moderate
Hayleigh	36	Pre	White	4 years	Discontinued (for fertility reasons)	None
Jenny	62	Unsure	Black British	1 year	Adherent	Severe
Julie	61	Post	White	6 years	Adherent	None
Ellen	50	Pre	White	2 years	Adherent	None
Miriam	41	Post	Asian / British	5 years	Non-adherent	Moderate / Severe
Michelle	77	Post	White	2 years (then switched)	Adherent	Moderate / Severe
Shannon	55	Post	Asian / British	5 years	Adherent	Mild

Frances	77	Post	White	2 years, 2 months	Adherent	None
Anna	60	Post	White	2 years	Adherent	None
Lucy	53	Post	Black British	5 years	Adherent	Mild
Lauren	62	Post	White	18 months	Adherent	Mild / Moderate
Dominique	45	Unsure	Black British	3 years	Adherent	Mild
Joanna	46	Unsure	Black British	1 year, 2 months	Adherent	Mild
Barbara	64	Post	White	1 year	Non-adherent	Mild / moderate
Vanessa	63	Post	White	2 years	Adherent	Mild
Kate	52	Pre	White	14 months	Non-adherent	Moderate
Lorena	58	Post	White	1 year	Discontinued (due to blood clots)	Moderate / Severe
Bonnie	61	Peri	White	4 years 8 months	Discontinued	Severe
Tania	54	Peri	British Indian	1 year, 6 months	Adherent	Moderate
Claudia	60	Post	White Mixed	1 year	Adherent	Mild
Rosalind	44	Unsure	Black / British	7 months	Adherent	Mild
Anita	50	Peri	White	2 years	Discontinued	Severe
Marcia	54	Unsure	White	2 months	Adherent	None
Celia	67	Post	White	7 months	Non-adherent	Moderate / Severe

Results

Thirty two women were interviewed. Interviews lasted on average 44 minutes (range 16-81). Twenty-three women were classed as adherent, four were non-adherent and five had discontinued. Two of the women discontinued on their doctors' recommendations; one due to blood clots and one so that she could conceive.

Figure 1 shows the themes and subthemes identified in the data. A key theme for all women was the process of *weighing up costs and benefits of treatment*, which first consisted of *moving from initial acceptance of treatment*, and then resulted in women largely falling into one of three groups; *tamoxifen is keeping me alive*; *tamoxifen is not worth the reduced risk of recurrence*; or *conflicting beliefs around the harms and benefits of treatment*. Additional themes were *living with increased risk of recurrence* and *information & support*, both of which contributed to women's beliefs about treatment and how they weighed these beliefs up. Each of these themes and corresponding subthemes will be discussed in turn.

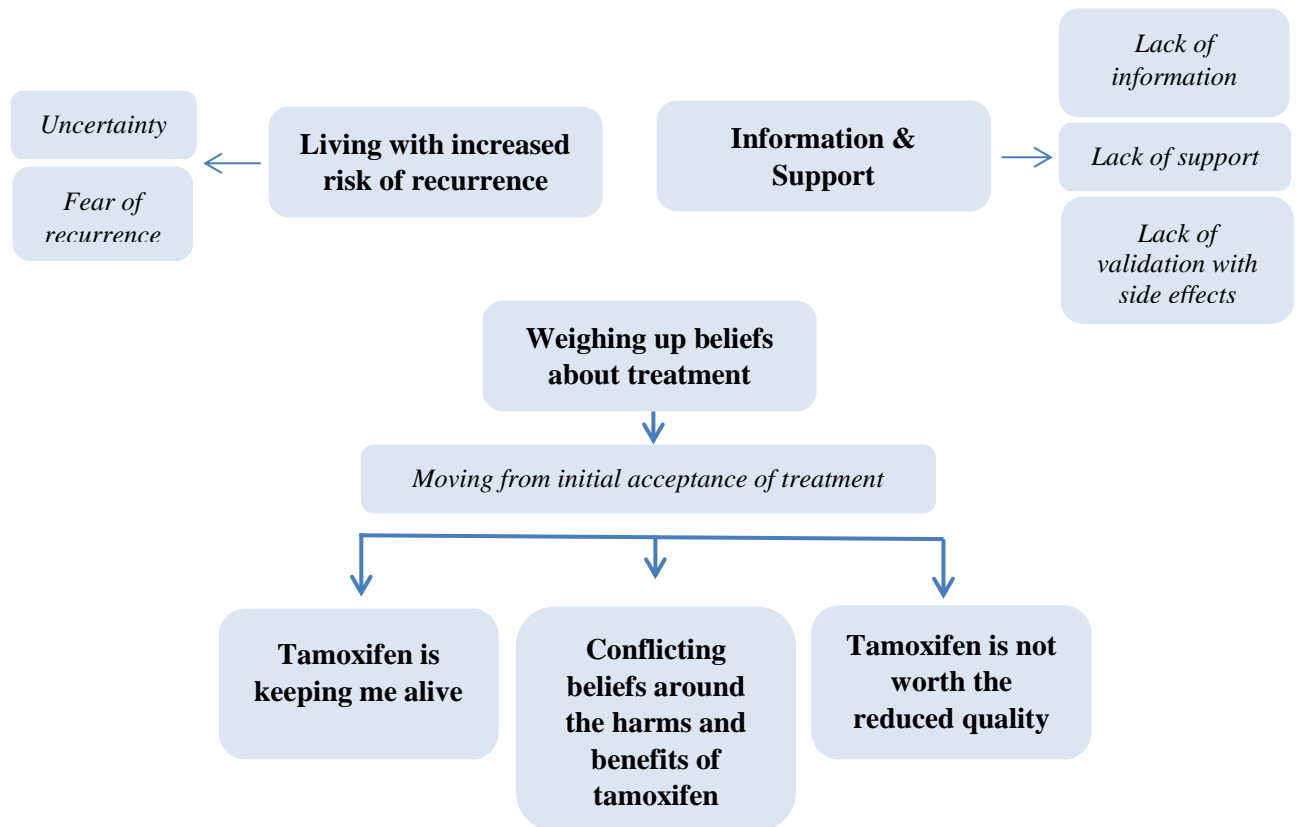


Figure 1: Themes and subthemes identified in the data. Themes are represented by bold text and subthemes by italic text.

Weighing up costs and benefits of treatment

Moving from initial acceptance of treatment. When the women were first prescribed tamoxifen, they are happy to follow whatever treatment their healthcare professional (HCP) recommended.

“It wasn't a choice at all. I mean they're professionals so I just listened to what they said.” (Barbara, 64, non-adherent)

However, over time, some women begin to question these initial beliefs and weigh them up against what it is actually like to take tamoxifen. This resulted in women falling into

one of three groups; those who held beliefs that tamoxifen was keeping them alive; those who felt that the benefits of tamoxifen were not worth the reduced QOL and those who had conflicting beliefs around the harms and benefits.

Tamoxifen is keeping me alive

Many patients held very strong beliefs regarding the necessity of taking tamoxifen. They felt it was incredibly important to take it every day. Whilst some patients spoke about wanting to avoid going through cancer treatment again, others were more motivated by a fear of death. Some women were also driven specifically by a desire to stay alive for their children.

“Well since the option is keep taking it or be dead, it’s not much of a choice for me.” (Vanessa, 63, adherent)

Some participants were less certain about the efficacy of tamoxifen, but they still felt it was necessary for them to keep taking it.

“Whether like you say with me it would have come back, I just don’t know. I’d rather take it than not.” (Ellen, 50, adherent)

As well as necessity beliefs, some women held strong beliefs regarding the control tamoxifen gave them over their risk of recurrence. They liked the fact that tamoxifen was a preventive measure and that it made them feel that they were actively doing something to prevent the cancer returning.

“[taking tamoxifen] makes me feel better as well, because I feel like I am doing something actively to prevent it.” (Joanna, 46, adherent)

For some women these control beliefs were so strong that they were concerned about what would happen when their prescription ended.

“In one way I was quite looking forward to stopping, but then as it got nearer, I thought, ooh, it’s like a safety blanket being taken away isn’t it?” (Julie, 61, adherent)

Most women with strong necessity and control beliefs felt that they far outweighed any concerns they had. They were willing to experience some side effects if it meant they could stay alive and stop the cancer coming back.

“Taking tamoxifen just kind of pales into insignificance and it seems like a very small price to pay for not getting breast cancer again.” (Katie, 56, adherent)

The majority of these women were experiencing no side effects or mild side effects. However, some did have side effects which impacted on their QOL, including anxiety, forgetfulness, reduced libido and hot flushes. Despite this, they were willing to keep taking tamoxifen as their beliefs around the necessity of tamoxifen and their desire to stay alive was so strong.

“I never stopped taking it because I thought the nausea and things like that, come on its keeping you alive so stop moaning.” (Michelle, 77, adherent)

In order to help them cope with the side effects, many of these women developed coping strategies, such as meditating, removing layers of clothing and exercising. Whilst the majority of women who were adherent had positive views around tamoxifen and were happy to keep taking the medication, one woman disconfirmed this by having negative emotions and beliefs about tamoxifen, yet continuing to take it. She felt that

tamoxifen was a reminder of the fact that despite finishing her primary treatment, she still cannot get on with her life.

“I absolutely hate taking this tablet. It’s a very powerful drug. It’s not just the side effects. It’s a reminder of what I had.” (Lauren, 62, adherent)

Despite this strong dislike of taking tamoxifen, this patient’s necessity beliefs and fear of recurrence were strong and she therefore made sure she took tamoxifen every day.

“I’d be too frightened to be honest not to take it.” (Lauren, 62, adherent)

Taking tamoxifen is not worth the reduced quality of life

Whilst some patients had strong necessity beliefs which outweighed their side effects, others felt that the benefits of taking tamoxifen were outweighed by the severe side effects they were experiencing, which led them to discontinue treatment.

“I just couldn’t survive anymore taking it. My side effects were so bad I couldn’t work...When I stopped and realised the difference, there was no way I was going back on it.” (Bonnie, 61, discontinued)

Patients talked about not having enough energy to participate in their lives. They could not maintain relationships with family members and withdrew from social activities. Due to side effects like severe fatigue and depression, tamoxifen had a huge impact on their sense of self, causing them to feel like completely different people.

“When I was on tamoxifen, I was basically stuck in bed or sitting on the sofa feeling very sorry for myself. Just totally different person completely.” (Anita, 52, discontinued)

Two women also experienced severe depression and suicidal thoughts. Depression was attributed more to the overall impact of the side effects, which mainly included fatigue, insomnia and muscle cramps, than directly to tamoxifen.

“I can’t say that tamoxifen in itself was affecting my moods, but the repercussions of how it [the side effects] affected my life, again it’s hard to unpick which was having the most effect; was it the drug itself or was it just the repercussions of taking it?” (Bonnie, 61, discontinued)

One woman had a strong perception that tamoxifen was causing her to feel suicidal and she felt that this was the tipping point for her to discontinue.

“I felt so low, was having suicidal thoughts, really didn’t feel like myself at all, I was in so much pain and that I’d made the decision that I was going to come off tamoxifen.” (Anita, 52, discontinued)

These patients received little support from their healthcare teams in how to deal with the side effects, which exacerbated the impact on their lives. HCPs failed to acknowledge that the symptoms they were experiencing were related to tamoxifen and therefore did not offer any assistance.

“I actually was made to feel as if I was having like a mental breakdown...I don’t feel as if I was supported properly.” (Anita, 52, discontinued)

These women still felt that tamoxifen was an effective treatment for reducing a risk of recurrence, but they no longer felt that the benefits of treatment were worth the side effects and the impact on their QOL. Participants were confident that they had made the right decision and were willing to risk the chance of a recurrence or death in order to improve their immediate QOL.

“I thought actually I would rather be myself for however long that is, rather than be miserable for a longer period, and depending on what... whether the recurrence might occur or not I just thought well I’ll take that chance.” (Sylvie, 52, discontinued)

Conflicting beliefs around the harms and benefits of tamoxifen

Other patients had conflicting beliefs around the harms and benefits of tamoxifen. They were in turmoil trying to weigh up these beliefs, and to select a behavioural outcome to avoid cognitive dissonance. Many of these women made the decision to skip or halve doses of tamoxifen.

“I’ve got to the stage where sometimes I’ll just give it a miss...I just get so fed up of taking it, I just want to give myself a break.” (Miriam, 41, non-adherent)

These patients were struggling to cope with side effects such as fatigue, joint pain, hot flushes and weight gain, which were having a severe impact on their QOL.

“It [tamoxifen] is horrible. It really is the most revolting tablet I’ve ever had to take.” (Kate, 52, non-adherent)

As well as struggling to cope with side effects, patients also had concerns about the increased risk of cancer elsewhere.

“I worry more, not about the recurrence, but occurrence in a different part of my body due to this drug that I’m taking.” (Miriam, 41, non-adherent)

In addition to this, women struggled with negative emotions around tamoxifen. For example, some women saw tamoxifen as a reminder of having had cancer, others had negative feelings relating to the impact of cancer treatment on their fertility and some

had strong negative feelings about tamoxifen due to their experience of side effects. These negative emotions caused women to attribute a lot of their symptoms to tamoxifen.

“It is a hard drug to take because of everything it does. You think tamoxifen’s done that, and I do blame it for a lot of things.” (Kate, 52, non-adherent)

Despite these side effects, women wanted to keep taking tamoxifen to reduce their risk of recurrence.

“If it was for anything else other than the cancer I would have stopped it, there’s no questions, but because of the cancer is such a big thing, you know the possible return of it, that’s the only reason I’m struggling with it” (Celia, 67, non-adherent)

However they were equally as concerned about the side effects and their reduced QOL.

“But it’s like you’re damned if you do and you’re damned if you don’t. It’s that worry if you don’t take it, oh god, if they find something again then I think it’s because I didn’t take the tamoxifen. But on the other hand it’s living with all these side effects on it.” (Kate, 52, non-adherent)

Modifying their dosage allows the patient to feel like they are doing something to prevent the risk of cancer returning, but also allows them to exert some control over side effects. However, some patients felt guilty when they missed doses and ultimately resumed treatment if the guilt was too much, or if the fear of recurrence became too strong.

“When I don't take it I think oh, god, I should be taking it. I just feel so guilty when I don't take it, but I do feel better when I'm not on it.” (Kate, 52, non-adherent)

Information & support

Lack of information. Some patients felt that they were not always given enough information when prescribed tamoxifen. They had to do their own research on what to expect. Some had very basic knowledge around what tamoxifen was or why they were taking it.

“I didn't know anything about it. Really no one's sort of explained what it is. They just said tamoxifen will help stopping recurrence.” (Arlene, 62, adherent)

How informed women feel about tamoxifen is likely to influence how necessary or important they feel it is, which feeds in directly to the previous theme of *weighing up beliefs about treatment*. Additionally, women felt that if they had been told about what side effects to expect they would have been more prepared, which could then improve their management and experience of side effects, potentially reducing the numbers of women who discontinue treatment.

Lack of support. Many women did not feel that they received the support they needed from their HCPs in dealing with the side effects. They would have liked to have been warned about how bad they could be and given emotional support in dealing with them. This is also linked to the previous theme of *weighing beliefs about treatment*, as this support may have helped women who were struggling with side effects, potentially leading them not to discontinue treatment or skip doses.

“I think there should be more help, psychologically, with side effects of tamoxifen. I think people ought to be warned.” (Kate, 52, non-adherent)

Some patients went back to their breast clinic or GP for help with their side effects, but were not offered any practical coping strategies for how to reduce the impact of the side effects on their QOL. Patients also wanted more long term monitoring and support whilst they were taking tamoxifen.

“I would like there to be more help for people who get this extreme fatigue, whether it's from the radiotherapy or tamoxifen.” (Celia, 67, non-adherent)

Lack of validation with side effects. Some HCPs dismissed or belittled the side effects women were experiencing. Patients were told that their symptoms were not associated with tamoxifen, which left them feeling invalidated and frustrated.

“This is the one thing that I do find a lot of women struggling most with, that they feel so...they're just not listened to. They're not being validated in what they're experiencing.” (Bonnie, 61, discontinued)

Furthermore, some patients also felt that their families did not fully appreciate the extent of their side effects and thought the effects of tamoxifen were just linked to previous breast cancer.

“I really do think my family thought that I had fallen into a depression and everything just because of the cancer. I think they thought that I thought I was going to die or I just was full of doom and gloom. But it was just out of my control really.” (Anita, 52, discontinued)

Living with increased risk of recurrence

Fear of recurrence. Whilst most women did not identify as still having cancer, nearly all spoke about living in fear of cancer returning. They did not let this fear impact on their daily life, but said it would always be at the back of their mind. Some were not able to relax and were concerned that any little problem might be a sign of cancer.

“I find it very difficult to be honest...I think the thing is anything that you find that you feel that is not right in your body then you start thinking ‘I wonder if it’s something serious’.” (Arlene, 62, adherent)

This fear of recurrence relates to how necessary women feel that tamoxifen is for them, which then plays a key role in whether or not they adhere to treatment. Women who fell into the *tamoxifen is keeping me alive* group spoke about being motivated by avoiding a recurrence. Women who felt that *tamoxifen was not worth the reduced QOL* were less concerned about a recurrence than they were by their side effects. Most women said that they tried to block out this fear and not think about it. Some cited taking tamoxifen as a way to help them control it. Others talked about making changes to their lifestyle to try and be healthier. A few women felt that there was nothing they could do to control the risk of recurrence.

“That would be my biggest fear is, it’s not, I suppose if it’s going to come back it’s possibly when, but I can’t live my life like that. So I kind of like have to block it and just continue as much as I can.” (Elisabeth, 37, adherent)

Uncertainty about recurrence. Participants reflected on the uncertainty of cancer regarding why it comes back or whether it will come back. They said this uncertainty and fear was hard to deal with.

“Someone said to me it’s like having a sword dangling above your head, and it is. You just feel like tomorrow you don’t know what’s going to happen. It’s always there in the back of your mind.” (Kate, 52, non-adherent)

For women who were trying to decide whether or not to take tamoxifen, this uncertainty made it harder for them to make a decision.

“I can never know what the right answer is, because I don’t know whether the cancer will come back. I can’t know until it happens.” (Celia, 67, non-adherent)

Women who had discontinued tamoxifen were happy in their decision because they said they wouldn’t be able to guarantee that they wouldn’t have a recurrence of cancer even if they were taking tamoxifen.

“I’ll have to deal with that if it happens, and the thing is you’ve no idea, you have no way of knowing if it would’ve happened anyway. I’m happy enough”
(Bonnie, 61, discontinued)

Discussion

These results provide insight into the experiences of patients who initiated tamoxifen. Initially, women in this study were happy to take tamoxifen and did not question the doctor’s decision. Over time, however, they weighed up the benefits of taking tamoxifen against the harms, leading to some patients becoming non-adherent or non-persistent. Women who felt that the necessity of taking tamoxifen far outweighed the side-effects were more likely to be adherent. Women who felt that the side effects were not worth the benefits were more likely to self-report discontinuing treatment. Some women were struggling to cope with the side effects but did not want to discontinue treatment due to their strong beliefs in the necessity of tamoxifen. In order to cope with

this and control the side effects, they skipped or halved doses. Patients in this study fell into one of these three distinct groups, but this may not generalise to all women.

Whilst some women were happy with their decision to discontinue treatment, and felt it was the right choice for them, others were keen to continue treatment but were struggling with side effects, and some did not fully understand how tamoxifen helps them. These latter two groups may benefit from interventions informed by the results of this study, such as detailing how tamoxifen works to reduce recurrence or self-management and support for side effects. Furthermore, if we can intervene early to support women with side effects, we may be able to prevent patients reaching the stage where it is no longer worth it for them to take tamoxifen.

Many patients felt that they were not given enough information about tamoxifen. If women went to their HCPs for help, they were often not given support in managing their side effects. Additionally, some women felt that their HCPs did not validate their experience of side effects. Side effects were consistent with what has been documented in previous literature (Boehm et al., 2009; Garreau, Delamelena, Walts, Karamlou, & Johnson, 2006). Some side-effects had a significant impact on women's QOL, prohibiting them from working or socialising. The majority of women did not know how to manage these side effects, which exacerbated their impact on social, physical and emotional functioning. In extreme cases, the accumulation of unmanaged side effects led to patients feeling depressed and suicidal.

Whilst the data was analysed using an inductive approach and a reflexive process was used to avoid any pre-conceived knowledge and biases, the themes that were generated fit well within the Self-Regulation Model of Illness Perceptions (Leventhal, Diefenbach,

& Leventhal, 1992) and the Necessity Concerns Framework (Horne & Weinman, 1999). Illness perceptions, such as perceptions around the risk of recurrence, do seem to impact on adherence, as do beliefs about the necessity of tamoxifen. The Necessity-Concerns Framework suggests that when deciding whether to take medication, patients weigh up their concerns against their beliefs regarding how necessary the medication is for them (Horne & Weinman, 1999). These beliefs have been shown to relate to HT adherence and persistence (Fink, Gurwitz, Rakowski, Guadagnoli, & Silliman, 2004; Jacob Arriola et al., 2014). This study contributes new understanding by moving beyond the generic model and showing the specific beliefs held by these patients and how they influence behaviour. It highlights the strength of some women's necessity beliefs and shows the variability of the cost-benefit analysis across women; some women's desire to stay alive were so strong that they reported tolerating any side effects whereas others would rather not live with the side effects despite the risk of recurrence. Women may hold such strong necessity beliefs because the outcome of not taking the medication is so serious.

Women also had concerns about tamoxifen, but these seemed to focus almost exclusively on the experience of side effects, rather than other common concerns such as dependency. The beliefs women held were also consistent with the Self-Regulation Model of Illness Perceptions (Leventhal, Diefenbach, & Leventhal, 1992), which proposes that coping behaviours such as adherence are influenced by patient's beliefs about their illness (Chilcot, Wellsted, & Farrington, 2010). Patients in this study held strong beliefs regarding the extent to which tamoxifen could control their risk of cancer. The results of this study give interesting insight into the specific illness perceptions held by breast cancer survivors taking tamoxifen. These women did not perceive themselves

as currently having cancer, but did feel at risk of a recurrence and struggled to cope with the uncertainty surrounding this. This fear of recurrence is what motivated women to continue taking their tamoxifen.

This study suggested that side effects can cause women to discontinue treatment, which has been shown in several quantitative studies (Demissie, et al., 2001; Simon, Latreille, Matte, Desjardins, & Bergeron, 2014; Wouters et al., 2014). However, there is an inconsistent relationship between side effects and adherence, with some studies finding no significant effects (Fink, et al., 2004; Kostev et al., 2013). The results from this study suggest that adherence is not just related to the experience of side effects, but how women weigh these up against their beliefs; that is that just the experience of side effects is not sufficient to cause non-adherence. This may explain the inconsistent effects found previously. Furthermore, adherence rates may be related more to the perceived impact of side effects, than the side effects themselves as evidenced by the fact that nearly all of the women experienced side effects to some extent but most persisted with their tamoxifen treatment. This weighing up process is also supported by trade-off studies showing that women with more severe side effects needed larger gains in survival to make HT worthwhile (Duric et al., 2005; Thewes et al., 2005).

Previous research has suggested that forgetting is a significant driver in HT non-adherence (Atkins & Fallowfield, 2006). However in this study, forgetting did not seem to be a problem for women. Women who felt that the benefits of tamoxifen outweighed the side effects were motivated to keep taking it every day and established routines which helped them to remember. Women who missed doses reported doing so deliberately, such as taking breaks when on holiday or skipping doses to avoid side effects. Although this is based on self-reported responses and should be treated with

caution, non-adherence through forgetting is often more commonly self-reported than deliberately skipping or changing doses. This could be due to socially-desirable reporting and the perception that forgetting is more “acceptable” than deliberately not following a prescription (Atkins & Fallowfield, 2006).

Some women did not feel that the benefits of tamoxifen were worth the reduced QOL, which may be related to the fact that the benefits are hidden and there is no reduction in symptoms which can be attributed to medication taking (Meyer, Leventhal & Gutmann, 1985). The information women receive about their treatment and side effects is therefore incredibly important in increasing their necessity beliefs. All women should be given personalised information, so they are able to make decisions about tamoxifen based on the extent to which it will benefit them. Women also wanted to be warned about what side-effects to expect. Previous research has shown that women who experienced side effects they were not told about were significantly more likely to discontinue HT (Kahn, Schneider, Malin, Adams, & Epstein, 2007). Furthermore, women who receive less information about HT are less likely to initiate treatment (Friese et al., 2013) and more likely to take treatment breaks (Cluze et al., 2012).

Patients also need to be informed about the importance of taking tamoxifen as prescribed. Some women deliberately missed or halved doses and still wanted to appreciate the benefits of tamoxifen. These women may not be aware that by reducing the dosage of tamoxifen they are reducing the effectiveness (McCowan, et al., 2008). If they were more educated about the implications of taking less than 80% of the prescribed dose, they may be more motivated to take it as prescribed.

Qualitative research provides a unique opportunity to understand a clinical problem from the patient's perspective. This study had a large diverse sample, recruited through a range of locations and used in-depth interviews which enhance the richness and generalisability of the results. However, there were several limitations. Firstly, women who had chosen not to initiate tamoxifen were not included in the study. Future research should interview these women to understand the reasons behind their decision. Second, the study may have under-represented women who were non-adherent as there may be a selection bias where non-adherent women were less likely to respond to advertisements. However, there is reason to believe that women with negative experiences may also be biased to respond to advertisements. Twenty nine percent of participants were either non-persistent or non-adherent, but research shows this figure could be as high as 50% (Partridge, Wang, Winer, & Avorn, 2003). Including more women who were non-adherent or non-persistent may have given further insights into what drives these behaviours. However, interviewing adherent women gives interesting insight into what motivates women to keep taking treatment, even when they are experiencing severe side effects. Finally, several of the women in the study had discontinued tamoxifen or had been taking it for some time and there may be issues of recall bias.

Clinical implications

Women who are given clear information about tamoxifen and how it might personally benefit them are in a much better position to make a decision on whether it is worth it for them to take it. Whilst for some women it is a logical choice to discontinue tamoxifen, others are keen to continue treatment but cannot cope with the side effects. Supporting these women may stop them from reaching the point where they have to discontinue. For women who are not fully informed, increasing necessity beliefs by

providing information may help to improve adherence rates and allows women to make an informed decision about continuing treatment. Patients should also be informed about the importance of taking tamoxifen as prescribed.

Conclusions

This study suggests that the main reason women are non-adherent or non-persistent with tamoxifen is because they are struggling with the side effects and they do not believe that the benefits of the treatment outweigh the side effects. Women expressed a need for more information about tamoxifen. Supporting women with their side effects and providing more information on the benefits of tamoxifen should help to increase adherence and improve clinical outcomes.

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